

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

- Claim 1. (Currently Amended) A method for preparing a recombinant minimal adenoviral vector stock comprising:
- (a) Introducing in a first cell line (i) a first helper adenoviral vector or virus and
 - (ii) a second helper adenoviral vector or virus, the genomes of both (i) and (ii) comprising 5' and 3' ITRs, an a encapsidation region and one or more gene(s) of the early and late regions, wherein the genome of (i) is obtained from a first adenovirus genome,
 - wherein the genome of (ii) is obtained from a second adenovirus genome with the exception of at least the encapsidation region which is obtained from said first adenovirus genome,
 - wherein said first helper (i) is capable of packaging said second helper (ii) is in said first cell line; and
 - wherein said first adenovirus genome is an animal adenovirus genome and said second adenovirus genome is a human adenovirus genome;
 - (b) culturing the cell obtained in step (a) under appropriate conditions to allow the production of viral particles comprising (ii)

- (c) recovering the viral particles obtained in step (b) from the cell culture,
- (d) introducing in a second cell line said viral particles obtained in step (c) and a recombinant minimal vector,
- (e) culturing the cell obtained in step (d) under appropriate conditions to allow the production of viral particles comprising said recombinant minimal vector, and
- (f) recovering the viral particles obtained in step (e) from the cell culture.

Claim 2. (Canceled)

Claim 3. (Currently Amended) The method of claim 1, wherein said first adenovirus genome is a bovine adenovirus genome and said second adenovirus genome is a human adenovirus genome.

Claim 4. (Currently Amended) The method of claim 3, wherein said first adenovirus genome is a BAV3 genome and said second adenovirus genome is an Ad5 genome.

Claim 5. (Canceled)

Claim 6. (Currently Amended) The method of claim 1 3, wherein said first helper (i) or said and/or second helper (ii) and said first helper (i) and said second helper (ii) adenoviral vector is (are) a defective mutant(s) of a wild-type adenovirus genome.

Claim 7. (Currently Amended) The method of claim 6, wherein said first and second helpers (i) and (ii) helper adenoviral vectors are defective mutants of wild-type adenovirus genomes and are capable of cross-complementing each other for at least one defective function.

Claim 8. (Currently Amended) The method of claim 6, wherein said first helper (i) adenoviral vector is defective for E1 function.

Claim 9. (Currently Amended) The method of claim 6, wherein said first helper (i) adenoviral vector is defective for in E2 function.

Claim 10. (Currently Amended) The method of claim 9, wherein said defective E2 function is caused by a mutation or deletion in one or more of at least the genes selected from the group consisting of the genes gene encoding DBP, Pol and and/or pTP.

Claim 11. (Currently Amended) The method of claim 6, wherein said second helper (ii) adenoviral vector is defective for E1 function.

Claim 12. (Currently Amended) The method of claim 11, wherein said second adenoviral helper (ii) heper vector is an Ad5 genome deleted of nucleotides approximately 455 to approximately 3327 and having nucleotides approximately 149

to approximately 454 comprising the Ad5 encapsidation region replaced by nucleotides approximately 141 to approximately 984 of the BAV3 genome.

Claim 13. (Currently Amended) The method of claim 1, wherein said second helper (ii) adenoviral vector is functional for the E1 function and contains an ~~wherein the E1 region of the adenoviral vector~~ providing said E1 function is placed under the control of a non-adenoviral promoter.

Claim 14. (Currently Amended) The method of claim 1, wherein said first and second helpers (i) and (ii) adenoviral helper vectors have an origin of replication recognized by the same E2-encoded gene products.

Claim 15. (Currently Amended) The method of claim 14, wherein the endogenous 5' and 3' ITRs of the first adenoviral helper (i) vector are modified to make the origin of replication recognized by the E2 gene products expressed from the second adenoviral helper (ii) vector.

Claim 16. (Currently Amended) The method of claim 15, wherein said modification consists in the replacement of:

- the penultimate 20 bp containing the core origin,
 - the penultimate 50 bp containing the entire origin of replication or
 - the entire ITRs
- of said first adenoviral helper (i) vector by:
- the penultimate 20bp containing the core origin

- the penultimate 50bp containing the entire origin of replication, or
- the entire ITRs

of the 5' and 3' ITRs of said second ~~adenoviral helper (ii) vector~~.

Claim 17. (Currently Amended) The method of claim 14, wherein the endogenous 5' and 3' ITRs of the second ~~adenoviral helper (ii) vector~~ are modified to make the origin of replication recognized by the E2 gene products expressed from the first ~~adenoviral helper (i) vector~~.

Claim 18. (Currently Amended) The method of claim 17, wherein the endogenous 5' and 3' ITRs of said second helper ~~(ii) adenoviral vector~~ are replaced by the 5' and 3' ITRs of said first adenovirus genome.

Claim 19. (Currently Amended) The method of claim 18, wherein said second helper ~~(ii) adenoviral vector~~ is an Ad5 genome deleted of nucleotides approximately 455 to approximately 3327 and nucleotides approximately 28592 to approximately 30470 and having nucleotides approximately 1 to approximately 454 comprising the 5' ITR ~~5'~~ and the Ad5 encapsidation region replaced by nucleotides approximately 1 to approximately 984 of the BAV3 genome and nucleotides approximately 35826 to approximately 35935 comprising the 3' ITR ~~3'~~ replaced by nucleotides approximately 34188 to approximately 34446 of the BAV3 genome.

Claim 20. (Previously Presented) The method of claim 1, wherein said first cell line is a non-human cell line.

Claim 21. (Currently Amended) The method of claim 20, wherein said first cell line has a bovine origin and wherein said first ~~adenoviral helper (i) vector is or~~ obtained from a BAV 3 genome.

Claim 22. (Currently Amended) The method of claim 20, wherein said first cell line is capable of complementing part of all of at least one defective function of a helper vector selected from the group consisting of the first helper (i), the second helper (ii) and the first and second helpers (i) and (ii)~~said first or second or first and second helper(s).~~

Claim 23. (Currently Amended) The method of claim 22, wherein said first cell line complements ~~is complementing~~ the E1 function of a helper vector selected from the group consisting of the first helper (i), the second helper (ii) and the first and second helpers (i) and (ii)~~said first or second or first and second adenoviral helper vector(s).~~

Claim 24. (Previously Presented) The method of claim 1 wherein said second cell line is of human origin.

Claim 25. (Original) The method of claim 24 wherein said second cell line is capable of complementing part of all of at least one defective function of said recombinant minimal vector.

Claim 26. (Previously Presented) The method of claim 25, wherein said second cell line is a complementing cell line for Ad5 E1 function.

Claim 27. (Original) The method of claim 26, wherein said second cell line is selected among the group consisting of PER-C6 and 293.

Claim 28. (Currently Amended) The method of claim 1, which comprises an additional step following step (f) more than one amplification step, wherein said viral particles recovered obtained in step (f) are used to reinfect said second cell line in the presence of an additional quantity of fresh second adenoviral helper (ii) vector or virus.

Claim 29. (Previously Presented) The method of claim 1, which further comprises a purification step of the viral particles obtained in step (f).

Claim 30. (Previously Presented) The method of claim 1, wherein said viral particles obtained in step (f) are helper-free.

Claim 31. (Withdrawn) An animal adenovirus genome having modified 5' and 3' ITRs and wherein said modification consists in the replacement of:

- the penultimate 20 bp containing the core origin,
- the penultimate 50 bp containing the entire origin of replication or
- the entire ITRs
of said animal adenovirus genome by the homologue sequences of the 5' and 3' ITRs of a human adenovirus genome.

Claim 32. (Previously Presented) A viral preparation obtained according to the method of claim 1, wherein said viral preparation is helper-free.

Claim 33. (Original) A host cell comprising a viral preparation according to claim 32.

Claim 34. (Withdrawn) A pharmaceutical composition comprising a viral preparation according to claim 32.

Claim 35. (Withdrawn) A method for the treatment of disease by gene therapy or immunotherapy comprising administering an effective amount of the viral preparation according to claim 32 to a patient in need of such treatment.

Claim 36. (Currently Amended) The method of claim 1 wherein step (b) is replaced by the step of (b) comprising culturing the cell obtained in step (a) under appropriate conditions to allow the production of viral particles comprising (i).

Claim 37. (Currently Amended) The method of claim 11, wherein said second helper (ii) adenoviral vector is defective for E3 function.